

What is claimed is:

1. A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone antagonist polypeptide in genetically modified host cells, the process comprising the step of:
 - (a) contacting with said impurity under sufficient conditions a mercapto compound to decrease said amount of said impurity, wherein said impurity is a trisulfide isoform of said polypeptide.
2. The process of embodiment 1 further comprising the step of:
 - (b) growing said host cells to produce said polypeptide, wherein said growing is conducted either before or during said contacting step (a).
3. The process of embodiment 2 further comprising the step of:
 - (c) purifying said polypeptide to yield a purified polypeptide.
4. The process of embodiment 3 further comprising the step of:
 - (d) pegylating said purified polypeptide.
5. The process of embodiment 2 wherein said mercapto compound is selected from the group consisting of sulfites, glutathione, beta-mercaptoethanol, dithiothreitol, mercaptoethylamine, dithioerythritol, tris(2-carboxyethyl) phosphine hydrochloride, cysteine, and cysteine in combination with cystine.
6. The process of embodiment 1 wherein said mercapto compound is selected from the group consisting of sulfites, glutathione, beta-mercaptoethanol, dithiothreitol, mercaptoethylamine, dithioerythritol, tris(2-carboxyethyl) phosphine hydrochloride, cysteine, and cysteine in combination with cystine.
7. The process of embodiment 5 wherein said mercapto compound comprises cysteine or a combination of cysteine and cystine.

8. The process of embodiment 6 wherein said mercapto compound comprises cysteine or a combination of cysteine and cystine.
9. The process of embodiment 7 wherein in said contacting step (a), said trisulfide isoform is contacted with said cysteine or combination of cysteine and cystine for a period of time sufficient to decrease said amount of said trisulfide isoform by at least about 10%.
10. The process of embodiment 9 wherein said period of time is sufficient to decrease said amount of said trisulfide isoform by at least about 50%.
11. The process of embodiment 8 wherein in said contacting step (a), said trisulfide isoform is contacted with said cysteine for a period of time sufficient to decrease said amount of said trisulfide isoform by at least about 10%.
12. The process of embodiment 11 wherein said period of time is sufficient to decrease said amount of said trisulfide isoform by at least about 50%.
13. The process of embodiment 1 wherein said mercapto compound is provided in a buffer.
14. The process of embodiment 2 wherein said mercapto compound is provided in a buffer.
15. The process of embodiment 7 wherein said cysteine or combination of cysteine and cystine is provided in a buffer.
16. The process of embodiment 8 wherein said cysteine or combination of cysteine and cystine is provided in a buffer.
17. The process of embodiment 15 wherein before said contacting step (a), said buffer has an initial combined cysteine and cystine concentration of at least about 0.1 mM.

18. The process of embodiment 16 wherein before said contacting step (a), said buffer has an initial combined cysteine and cystine concentration of at least about 0.1 mM.
19. The process of embodiment 17 wherein said initial combined cysteine and cystine concentration is from about 0.1 mM to about 10 mM.
20. The process of embodiment 18 wherein said initial combined cysteine and cystine concentration is from about 0.1 mM to about 10 mM.
21. The process of embodiment 19 wherein said initial combined cysteine and cystine concentration is from about 1 mM to about 5 mM.
22. The process of embodiment 20 wherein said initial combined cysteine and cystine concentration is from about 1 mM to about 5 mM.
23. The process of embodiment 13 wherein said buffer is selected from the group consisting of Tris, phosphate, HEPES, citric acid, triethylamine, and histidine.
24. The process of embodiment 14 wherein said buffer is selected from the group consisting of Tris, phosphate, HEPES, citric acid, triethylamine, and histidine.
25. The process of embodiment 15 wherein said buffer is selected from the group consisting of Tris, phosphate, HEPES, citric acid, triethylamine, and histidine.
26. The process of embodiment 16 wherein said buffer is selected from the group consisting of Tris, phosphate, HEPES, citric acid, triethylamine, and histidine.
27. The process of embodiment 23 wherein said buffer comprises Tris.
28. The process of embodiment 26 wherein said buffer comprises Tris.

29. The process of embodiment 25 wherein said buffer comprises Tris.
30. The process of embodiment 24 wherein said buffer comprises Tris.
31. The process of embodiment 29 wherein after said contacting step (a) said Tris buffer has a Tris concentration from about 1 mM to about 200 mM.
32. The process of embodiment 28 wherein after said contacting step (a) said Tris buffer has a Tris concentration from about 1 mM to about 200 mM.
33. The process of embodiment 31 wherein said Tris concentration is from about 10 mM to about 50 mM.
34. The process of embodiment 32 wherein said Tris concentration is from about 10 mM to about 50 mM.
35. The process of embodiment 1 wherein said growth hormone antagonist polypeptide comprises B-2036 of [SEQ. ID. NO. 1].
36. The process of embodiment 2 wherein said growth hormone antagonist polypeptide comprises B-2036 of [SEQ. ID. NO. 1].
37. The process of embodiment 25 wherein said growth hormone antagonist polypeptide comprises B-2036 of [SEQ. ID. NO. 1].
38. The process of embodiment 26 wherein said growth hormone antagonist polypeptide comprises B-2036 of [SEQ. ID. NO. 1].
39. The process of embodiment 38 wherein before said contacting step (a), said buffer has an initial combined cysteine and cystine concentration of at least about 0.1 mM.

40. The process of embodiment 37 wherein before said contacting step (a), said buffer has an initial combined cysteine and cystine concentration of at least about 0.1 mM.
41. The process of embodiment 37 wherein said combination of cysteine and cystine in said buffer and said B-2036 before said contacting step (a) have a molar ratio of moles of combined cysteine and cystine to moles of B-2036 from about 0.5 to about 1000.
42. The process of embodiment 38 wherein said combination of cysteine and cystine in said buffer and said B-2036 and before said contacting step (a) have a molar ratio of moles of combined cysteine and cystine to moles of B-2036 from about 0.5 to about 1000.
43. The process of embodiment 37 wherein after said contacting step (a) said B-2036 in said buffer has a B-2036 concentration from about 0.1 mg/ml to about 30 mg/ml.
44. The process of embodiment 38 wherein after said contacting step (a) said B-2036 in said buffer has a B-2036 concentration from about 0.1 mg/ml to about 30 mg/ml.
45. The process of embodiment 43 wherein said B-2036 concentration is from about 0.5 mg/ml to about 20 mg/ml.
46. The process of embodiment 44 wherein said B-2036 concentration is from about 0.5 mg/ml to about 20 mg/ml.
47. The method of embodiment 45 wherein said B-2036 concentration is from about 1 mg/ml to about 10 mg/ml.
48. The method of embodiment 46 wherein said B-2036 concentration is from about 1 mg/ml to about 10 mg/ml.
49. The process of embodiment 37 wherein after said contacting step (a) said buffer has a pH from about 6 to about 9.

50. The process of embodiment 38 wherein after said contacting step (a) said buffer has a pH from about 6 to about 9.
51. The process of embodiment 49 wherein said pH is from about 7.5 to about 8.5.
52. The process of embodiment 50 wherein said pH is from about 7.5 to about 8.5.
53. The process of embodiment 37 wherein said buffer and said B-2036 are maintained at a temperature from about 0°C to about 25°C after said contacting step (a).
54. The process of embodiment 38 wherein said buffer and said B-2036 are maintained at a temperature from about 0°C to about 25°C after said contacting step (a).
55. The process of embodiment 53 wherein said temperature is from about 2°C to about 8°C.
56. The process of embodiment 54 wherein said temperature is from about 2°C to about 8°C.
57. The process of embodiment 37 wherein said contacting step (a) is conducted for a time of at least about 30 minutes.
58. The process of embodiment 38 wherein said contacting step (a) is conducted for a time of at least about 30 minutes.
59. The process of embodiment 57 wherein said time is from about 1 hour to about 24 hours.
60. The process of embodiment 58 wherein said time is from about 1 hour to about 24 hours.
61. The process of embodiment 59 wherein said time is from about 1 hour to about 4 hours.
62. The process of embodiment 60 wherein said time is from about 1 hour to about 4 hours.

63. The process of embodiment 37 wherein after said contacting step (a) said B-2036 in said buffer has a volume from about 1 L to about 5000 L.
64. The process of embodiment 38 wherein after said contacting step (a) said B-2036 in said buffer has a volume from about 1 L to about 5000 L.
65. The process of embodiment 63 wherein said volume is from about 10 L to about 500 L.
66. The process of embodiment 64 wherein said volume is from about 10 L to about 500 L.
67. The process of embodiment 65 wherein said volume is from about 100 L to about 300 L.
68. The process of embodiment 66 wherein said volume is from about 100 L to about 300 L.
69. A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone antagonist polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:
 - (a) contacting a chelating agent under sufficient conditions with (1) said impurity, (2) said growth hormone antagonist polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity,
wherein said impurity is a trisulfide isoform of said polypeptide.
70. A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone antagonist polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:
 - (a) contacting a metal salt under sufficient conditions with (1) said impurity, (2) said growth hormone antagonist polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity,

wherein said impurity is a trisulfide isoform of said polypeptide.

71. A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone antagonist polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:

(a) contacting a chelating agent under sufficient conditions with (1) said impurity, (2) said growth hormone antagonist polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity,

wherein said impurity is a des-phe isoform of said polypeptide.

72. A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone antagonist polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:

(a) contacting a metal salt under sufficient conditions with (1) said impurity, (2) said growth hormone antagonist polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity,

wherein said impurity is a des-phe isoform of said polypeptide.

73. A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:

(a) contacting a chelating agent under sufficient conditions with (1) said impurity, (2) said growth hormone polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity,

wherein said impurity is a des-phe isoform of said polypeptide.

74. A process for decreasing the amount of an impurity produced in recombinant production of a growth hormone polypeptide in genetically modified host cells containing cellular component(s), the process comprising the step of:
- (a) contacting a metal salt under sufficient conditions with (1) said impurity, (2) said growth hormone polypeptide, (3) said cellular component(s) and (4) combinations thereof to decrease said amount of said impurity, wherein said impurity is a des-phe isoform of said polypeptide.
75. The process of embodiment 73, wherein said contacting step (a) is conducted in the absence of a mercapto compound.
76. The process of embodiment 74, wherein said contacting step (a) further comprises contacting with said metal salt in combination with a mercapto compound.